REMARKS/ARGUMENTS:

Minor changes are made to this specification. Claim 5 is canceled without prejudice. Claims 1, 8, and 9 are amended. Support for the amendment to claim 1 can be found in claim 5. Claims 1 and 8-11 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

BRIEF DESCRIPTION OF THE FIGURES:

The Office states,

> "The Brief Description of the Figures remains objected because Figure 8 comprises part (a) and (b) to be labeled as Figure 8 (a)-(b) for the reasons of record on pg. 2 of the Office Action of 12/11/2009. Applicants argue that only they need to describe what Figure 8 (a) and (b) are in the Brief Description. This has been considered but not persuasive because the Brief Description should describe exactly what the figure legend says."

Applicant respectfully disagrees. As discussed in the June 10, 2010 amendment in response to the December 11, 2009 Office Action, the MPEP at 608.01(f) and 37 C.F.R. 1.74 only require that all of the views of the drawings be labeled and described. The specification on p. 6, at lines 25-29 provides a description of both views (a) and (b) that are shown in figure 8 of the drawings. As such, the Brief Description of Figures satisfies the necessary requirements.

Furthermore, Applicant respectfully submits that the Brief Description describes exactly what the figure legend says. The Brief Description at p. 6, lines 25-29 states,

> "Figure 8 shows that the recombinant fusion protein is recognized by anti-Tf and anti-G-CSF antibodies. (a) Western-blot using anti-Tf antibody. Lane A: fusion protein; lane B: transferrin. (b) Western-blot using anti-G-CSF antibody. Lane A: fusion protein; lane B: G-CSF control."

The above sentence "Figure 8 shows that the recombinant fusion protein is recognized by anti-Tf and anti-G-CSF antibodies" refers to both Figure 8a and Figure 8b. The sentence "(a) Western-blot using anti-Tf antibody. Lane A: fusion protein; lane B: transferrin" refers to Figure 8a; and the sentence "(b) Western-blot using anti-G-CSF antibody. Lane A: fusion protein; lane B: G-CSF control" refers to Figure 8b. Thus, the Brief Description describes exactly what is in the figure.

However, in order to expedite prosecution of the instant application, Applicant amended the Brief Description to refer to Figures "8a" and "8b". The sentence that referred to both Figures "8a" and "8b" (i.e., Figure "8") was modified to refer to Figures 8a and 8b individually. Withdrawal of this objection is thus respectfully requested.

CLAIM OBJECTIONS:

The Office states,

> "Claim 9 is objected because it recites 'wherein the order of the G-CSF domain and the Tf domain is from the N-terminus to the C-terminus' It is noted that all the proteins run from N-terminus to C-terminus. If Applicant meant to be that the G-CSF domain is N-terminus to the Tf, then the claim should be amended to 'wherein the G-CSF domain is N-terminus to the Tf domain'"

In response, Applicant amended claim 9 in the manner suggested by the Office. Withdrawal of this objection is thus respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §102:

Claims 1, 5, and 9-11 stand rejected under 35 U.S.C. §102(a) as being anticipated by Widera et al. (Pharmaceutical Res. 20: 1231-1238, 2003). This rejection is moot with respect to claim 5 due to the cancellation of this claim. Claim 5 is incorporated into claim 1. Applicant respectfully traverses this rejection as to claims 1 and 9-11.

Claim 1, as amended, is as follows:

> A fusion polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferrin (Tf) domain, wherein the ability of the polypeptide to be transported into a cell expressing a transferrin receptor (TfR) gene or the ability of the polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the G-CSF domain alone, wherein the polypeptide is a recombinant polypeptide.

Applicant respectfully submits that Widera cannot anticipate or render claim 1 obvious, because Widera fails to teach or suggest "a fusion protein" as set forth above "wherein the polypeptide is a recombinant polypeptide."

It is an aspect of the present invention that G-CSF-Tf fusion proteins may be produced in large quantities with a high degree of purity, exhibit a higher efficacy than a conjugate in a body or cell, remain intact in a cell or body, and have a longer half-life. In contrast, conjugates produce mixtures of heterogeneous protein aggregates and are thus impure, have lower half -lives and may dissociate inside a cell or body (Applicant's specification, at p. 23, line 25-p. 24, line 10).

The Office at p. 4, line 10-p. 5, line 1 states,

> "Applicants argue that the reference Widera cannot anticipate or render claim 1 obvious because the reference does not teach or suggest a fusion polypeptide comprising G-CSF and Tf. They argue that Widera does not teach any possible advantages a fusion protein may have over a conjugate. They argue that the specification on pg. 23 teaches advantages of a fusion protein over a conjugate. Applicants'

> arguments have been fully considered but they are not persuasive because the instantly claimed invention is drawn to a fusion polypeptide comprising a granulocyte colony stimulating factor domain operatively linked to a transferrin domain. The specification on page 1 lines 13+ discloses that the present invention relates to GCSF-transferrin fusion protein (e.g., conjugate and recombinant proteins). The specification on page 9 defines 'G-CSF-Tf fusion protein' as a composite protein containing both a G-CSF domain and a Tf domain. The reference Widera et al teaches a polypeptide conjugate comprising G-CSF and transferrin linked with a disulfide bond."

In response, Applicant amended claim 1 to further clarify that the fusion polypeptide is a recombinant polypeptide and is therefore, NOT a conjugate. Applicant's specification at p. 10, lines 20-31 states,

> "The G-CSF domain and the Tf domain can be physically or chemically linked. For example, the two domains may be linked through non-covalent bonding. In one embodiment, avidin may be attached to one of the domains and biotin to the other. In forming a fusion protein, the two domains are linked through avidin-biotin bridge. Alternatively, the two domains may be linked through covalent bonding. For example, cross-linking reagents may be used to generate a G-CSF-Tf fusion protein, e.g., as described in Example 1 below.
>
> The fusion protein may also be produced as a recombinant protein. In this case, a DNA encoding the fusion protein is constructed and transcribed into an mRNA. The mRNA is then translated into the fusion protein."

Therefore, as discussed above, a "recombinant protein" is not the same as a "conjugate", since the protein is not the result of domains being conjugated together. Instead, the protein is a result of the DNA encoding the fusion protein being constructed and transcribed into an mRNA, and the mRNA is then translated into the fusion protein."

Furthermore, Widera teaches away from the use of recombinant proteins. In Widera, a disulfide linker is used to link GCSF to Tf and form a GCSF-Tf conjugate. (Widera, p. 1232, column 2, lines 24-26). This disulfide linker is then used for releasing free active protein drug. Specifically, reduction of the labile disulfide

bonds within the linker moiety liberates free active protein drug from the conjugate. (Widera, p. 1237, column 2, lines 32-48). Therefore, based upon the teaching of Widera, a person of ordinary skill in the art would have no motivation to produce a recombinant protein, since the recombinant protein would not allow for the release of free active protein drug.

In light of the foregoing, Applicant respectfully submits that Widera cannot anticipate or render claim 1 obvious, because Widera fails to teach or suggest each and every claim limitation. Claims 9-11 depend from claim 1 and cannot be anticipated or rendered obvious for at least the same reasons as claim 1. Withdrawal of this rejection is thus respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §103:

Claims 1, 5, and 8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Widera in view of Prior et al. (U. S. Patent No. 7,176,278). This rejection is moot with respect to claim 5 due to the cancellation of this claim. Applicant respectfully traverses this rejection as to claims 1 and 8.

Claim 1 and its dependent claim 8 are patentable over Widera for reasons discussed above. Prior cannot remedy the defect of Widera and is not relied upon by the Office for such. Instead, the Office cites Prior for teaching a fusion protein between Tf and another protein.

In light of the foregoing, Applicant respectfully submits that the cited references cannot render claims 1 and 8 obvious, because the cited references fail to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

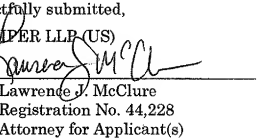
In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (310) 595-3107 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 07-1896.

Respectfully submitted,
DLA PIPER LLP (US)

Date: February 18, 2011

By: 
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